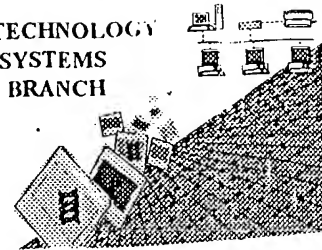


BIOTECHNOLOGY  
SYSTEMS  
BRANCH



## CRF Problem Report

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) experienced a problem when processing the following computer readable form (CRF):

Application Serial Number: 10/791,316  
Filing Date: 3/11/04  
Date Processed by STIC: 8/19/04

STIC Contact: Mark Spencer: Telephone: 571-272-2510; Fax: 571-273-0221

### Nature of Problem:

The CRF (was):

- ☐ (circle one) Damaged or Unreadable (for Unreadable, see attached)  
☐ Blank (no files on CRF) (see attached)  
☐ Empty file (filename present, but no bytes in file) (see attached)  
☐ Virus-infected. Virus name: \_\_\_\_\_ The STIC will not process the CRF.  
☐ Not saved in ASCII text  
☐ Sequence Listing was embedded in the file. According to Sequence Rules, submitted file should **only** be the Sequence Listing.  
☒ Did not contain a Sequence Listing. (see attached sample)  
☐ Other: \_\_\_\_\_

**PLEASE USE THE CHECKER VERSION 4.2 PROGRAM TO REDUCE ERRORS.  
SEE BELOW FOR ADDRESS:**

<http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<http://www.uspto.gov/efb/efs/downloads/documents.htm>) , EFS Submission User Manual - cPAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 06/05/04):  
U.S. Patent and Trademark Office, 220 20<sup>th</sup> Street S., Customer Window, Mail Stop Sequence, Crystal Plaza Two, Lobby, Room 1B03, Arlington, VA 22202

Revised 05/19/04

(Sample of submitted file)



10/791,316  
IFWO

49870/CAB/R2682

SK3-1B TRANSGENIC MOUSE MODEL FOR SPINOCEREBELLAR ATAXIA AND  
HYPEREXCITABLE BEHAVIOR

1

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

5

This invention was made with Government support under Grant  
No. NIH MH59222, awarded by the National Institutes of Health.  
The Government may have certain rights in this invention.

INTRODUCTION

10

15

20

25

Small conductance calcium-activated potassium (SK) channels,  
products of the SK1-SK3 genes, are critical modulators of calcium  
signaling, firing frequency and inter-spike interval in the  
brain. The SK3 channel has been implicated in dominant ataxia,  
schizophrenia and anorexia nervosa. The SK3 gene and protein are  
described in U.S. Patent No. 6,165,719, the entire contents of  
which are incorporated by reference. Recently, we have described  
the isolation of a novel SK3 splice variant, SK3-1 B, which  
encodes a truncated product that suppresses SK channels in a  
dominant-negative manner (See Attachment 1). Such molecular  
suppression of endogenous SK channels in the brain should enhance  
neural excitability and induce calcium mediated excitotoxicity,  
analogous to the effect of the SK channel blocking neurotoxin  
apamin. To test this idea, we generated transgenic mice  
over-expressing SK3-1B in the brain under control of Thyl.2-SX, a  
neuron-specific promoter. Eleven transgenic founders have been  
identified and of these seven exhibit progressively worsening  
ataxia, intention tremor, and hyper-excitable behavior. The  
symptoms started at the 7th-8th week of life and progressively  
worsened.

30

Table 1 (Attachment 2) summarizes the clinical phenotype of  
all eleven founders. We analyzed the gait of transgenic (Tg) mice  
using ink imprints. Mice were allowed to walk on an inkpad and  
then onto a sheet of white paper. In contrast to control